Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

Claim 1. (currently amended) A method of delivering a medicant to an abnormal brain region in a mammalian subject, comprising: administering to a mammalian subject having an abnormal brain region a direct agonist of an ~~in vivo activator of calcium-activated~~ ATP-sensitive potassium channel, ~~said activator being an activator of soluble guanylyl cyclase~~, under conditions and in an amount sufficient to increase the permeability to the medicant of a capillary or arteriole delivering blood to cells of the abnormal brain region; and administering ~~the medicant~~ to the subject, simultaneously or substantially simultaneously with the direct agonist ~~activator~~ the medicant, so that the medicant is delivered selectively to the cells of the abnormal brain region compared to normal brain regions.

Claim 2. (original) The method of Claim 1, wherein the abnormal brain region is a region of brain tissue physiologically affected by injury, trauma, infection, stroke or ischemia.

Claim 3. (currently amended) The method of Claim 1, wherein the abnormal brain region is a region of ~~benign or malignant~~ tumor tissue.

Claims 4-11 (cancelled)

Claim 12. (original) The method of Claim 1, wherein the mammal is a human~~, non-human primate, canine, feline, bovine, porcine, ovine, mouse, rat, gerbil, hamster or rabbit~~.

Claim 13. (currently amended) The method of Claim 1, wherein the medicant is a therapeutic cytotoxic agent~~, DNA expression vector, viral vector, protein, oligonucleotide, nucleotide analog, antimicrobial agent, interferon, cytokine, cytokine agonist, cytokine antagonist, immunotoxin, immunosuppressant, boron compound, monoclonal antibody, adrenergic agent, anticonvulsant, ischemia protective agent, anti-trauma agent,~~ or anticancer chemotherapeutic agent, ~~or diagnostic agent~~.

Claims 14-17 (cancelled)

Claim 18. (currently amended) The method of Claim 1, wherein ~~administering~~ the ~~activator~~ direct agonist is administered by intravenous or intra-arterial infusion or injection.

Claim 19. (currently amended) The method of claim 1, wherein ~~administering~~ the ~~activator~~ direct agonist is administered by intracarotid infusion or injection.

Claim 20. (currently amended) The method of Claim 1, wherein the ~~activator~~ direct agonist is administered to the mammalian subject by a ~~bolus injection~~ intravenous infusion.

Claim 21. (currently amended) The method of Claim 1, wherein the ~~activator~~ direct agonist is administered to the mammalian subject in an amount from about 0.075 to 1500 micrograms per kilogram body mass.

Claim 22. (currently amended) The method of Claim 21, wherein the ~~activator~~ direct agonist is administered to the subject in an amount from about 0.075 to 150 micrograms per kilogram body mass.

Claim 23. (currently amended) The method of Claim 1, wherein the ~~activator~~ direct agonist is administered to the mammalian subject at a dose rate of about 0.075 to about 100μg kg^{-1} min^{-1} for up to about 30 minutes.

Claim 24. (currently amended) The method of Claim 23, wherein the ~~activator~~ direct agonist is administered to the mammalian subject ~~at a dose rate of about 0.075 to about 15 μg kg-1 min-1.~~ in a bolus injection.

Claims 25-47 (cancelled)

Claim 48. (currently amended) A method of delivering a medicant to a malignant tumor in a mammalian subject, comprising: administering to a mammalian subject having a malignant tumor a direct agonist of an ~~in vivo activator of calcium-activated~~ ATP-sensitive potassium channel, ~~said activator being an activator of soluble guanylyl cyclase,~~ under conditions and in an amount sufficient to increase the permeability to the medicant of a capillary or arteriole delivering blood to cells of the malignant tumor; and administering ~~the medicant~~ to the subject, simultaneously or substantially simultaneously with the direct agonist ~~activator~~ the medicant, so that the medicant is delivered selectively to the malignant cells compared to non-malignant cells.

Claims 49-56 (cancelled)

Claim 57. (original) The method of Claim 48, wherein the malignant tumor is a glioma, glioblastoma, oligodendroglioma, astrocytoma, ependymoma, primitive neuroectodetermal tumor, atypical meningioma, malignant meningioma, neuroblastoma, sarcoma, melanoma, lymphoma or carcinoma.

Claim 58. (original) The method of Claim 48, wherein the malignant tumor is contained in the skull, brain, spine, thorax, lung, peritoneum, prostate, ovary, uterus, breast, stomach, liver, bowel, colon, rectum, bone, lymphatic system, or skin, of said subject.

Claim 9. (original) The method of Claim 48, wherein said mammal is a human~~, non-human primate, canine, feline, bovine, porcine, ovine, mouse, rat, gerbil, hamster or rabbit.~~

Claim 60. (original) The method of Claim 48, wherein the medicant is a therapeutic cytotoxic agent~~, DNA expression vector, viral vector, protein, oligonucleotide, nucleotide analog, antimicrobial agent, interferon, cytokine, cytokine agonist, cytokine antagonist, immunotoxin, immunosuppressant, boron compound, monoclonal antibody, adrenergic agent, anticonvulsant, ischemia protective agent, anti-trauma agent,~~ or anticancer chemotherapeutic agent~~, or diagnostic agent~~.

Claims 61-64 (cancelled)

Claim 65. (currently amended) The method of claim 48, wherein ~~administering~~ the ~~activator~~ direct agonist is administered by intravenous or intra-arterial infusion or injection.

Claim 66. (currently amended) The method of Claim 48, wherein ~~administering~~ the ~~activator~~ direct agonist is administered by intracarotid infusion or injection.

Claim 67. (currently amended) The method of Claim 48, wherein the ~~activator~~ direct agonist is administered to the mammalian subject by ~~a bolus injection~~ intravenous infusion.

Claim 68. (currently amended) The method of Claim 48, wherein the ~~activator~~ direct agonist is administered to the mammalian subject in an amount from about 0.075 to1500 micrograms per kilogram body mass.

Claim 69. (currently amended) The method of Claim 68, wherein the ~~activator~~ direct agonist is administered to the subject in an amount from about 0.075 to 150 micrograms per kilogram body mass.

Claim 70. (currently amended) The method of Claim 68, wherein the ~~activator~~ direct agonist is administered to the mammalian subject at a dose rate of about 0.075 to about 100μg kg^{-1} min^{-1} for up to about 30 minutes.

Claim 71. (currently amended) The method of Claim 70, wherein the ~~activator~~ direct agonist is administered ~~to the mammalian subject at a dose rate of about 0.075 to about 15 µg kg-1 min-1~~. by bolus injection.

Claims 72-134 (cancelled)

Claim 135. (currently amended) A pharmaceutical composition comprising a combination of ~~an in-vivo activator of calcium-activated potassium channel, said activator being an activator of soluble guanylyl cyclase~~ a direct agonist of an ATP-sensitive potassium channel, formulated in a pharmaceutically acceptable solution together with a medicant selected from the group consisting of therapeutic cytotoxic agents or anticancer chemotherapeutic agents for delivery by intravascular infusion or injection into a mammal.

Claim 136. (currently amended) The pharmaceutical composition of Claim 135, wherein the ~~solution is formulated to deliver a dose rate~~ direct agonist of an ATP-sensitive potassium channel is present in an amount of about 0.075 to 1500 micrograms ~~of the activator~~ per kilogram body mass ~~in a pharmaceutically acceptable fluid volume over a maximum of about thirty minutes~~.

Claim 137. (currently amended) The pharmaceutical composition of Claim 135, wherein the ~~solution is formulated to deliver a dose rate~~ direct agonist is present in an amount of about 0.075 to 150 micrograms ~~of the activator~~ per kilogram body mass ~~in a pharmaceutically acceptable fluid volume over a period of up to thirty minutes~~.

Claims 138-150 (cancelled)

Claim 151. (previously presented) The pharmaceutical composition of Claim 135, further comprising a buffer solution pharmaceutically acceptable for intravascular infusion into an animal.

Claim 152. (previously presented) The pharmaceutical composition of Claim 151, wherein the buffer solution is phosphate buffered saline.

Claim 153. (currently amended) A kit for enhancing the delivery of a medicant to an abnormal brain region and/or to a malignant tumor, comprising: a direct agonist of an ATP-sensitive potassium channel ~~an in vivo activator of calcium-activated potassium channel, said activator being an activator of soluble guanylyl cyclase;~~ and instructions for using the ~~activator~~ direct agonist for enhancing the delivery of a medicant to an abnormal brain region or to a malignant tumor.

Claims 154-189 (cancelled)

Claim 190. (new) The method of Claim 1, wherein the direct agonist is minoxidil or minoxidil sulfate.

Claim 191. (new) The method of Claim 1, wherein the direct agonist is cromakalim.

Claim 192. (new) The method of Claim 1, wherein the direct agonist is levcromakalim.

Claim 193. (new) The method of Claim 1, wherein the direct agonist is pinacidil.

Claim 194. (new) The method of Claim 1, wherein the direct agonist is diazoxide.

Claim 195. (new) The method of Claim 1, wherein the abnormal brain region is a region of brain tissue physiologically affected by stroke.

Claim 196. (new) The method of Claim 1, wherein the abnormal brain region is a region of brain tissue physiologically affected by ischemia.

Claim 197. (new) The method of Claim 1, wherein the abnormal brain region is a region of brain tissue physiologically affected by injury or trauma.

Claim 198. (new) The method of Claim 1, wherein the abnormal brain region is a region of brain tissue physiologically affected by infection.

Claim 199. (new) The method of Claim 1, wherein the abnormal brain region is a region of benign tumor tissue.

Claim 200. (new) The method of Claim 1, wherein the abnormal brain region is a region of malignant tumor tissue.

Claim 201. (new) The method of Claim 1, wherein the abnormal brain region includes a glioma, glioblastoma, oligodendroglioma, astrocytoma, ependymoma, primitive neuroectodermal

tumor, atypical meningioma, malignant meningioma, neuroblastoma, sarcoma, melanoma, lymphoma, or carcinoma.

Claim 202. (new) The method of Claim 1, wherein the medicant is administered via intravenous, intramuscular, intra-arterial, or intracarotid injection or infusion.

Claim 203. (new) The method of Claim 1, wherein the agonist and the medicant are administered via intracarotid infusion or injection.

Claim 204. (new) The method of Claim 1, wherein the medicant is a protein.

Claim 205. (new) The method of Claim 1, wherein the medicant is a monoclonal antibody or antigen-binding antibody fragment.

Claim 206. (new) The method of Claim 1, wherein the medicant is a cytokine, cytokine antagonist, or cytokine agonist.

Claim 207. (new) The method of Claim 1, wherein the medicant is an interferon.

Claim 208. (new) The method of Claim 1, wherein the medicant is an interleukin.

Claim 209. (new) The method of Claim 208, wherein the interleukin is interleukin 2.

Claim 210. (new) The method of Claim 1, wherein the medicant is transforming growth factor.

Claim 211. (new) The method of Claim 210, wherein the transforming growth factor is transforming growth factor-β

Claim 212. (new) The method of Claim 1, wherein the medicant is tumor necrosis factor-α.

Claim 213. (new) The method of Claim 1, wherein the medicant is an antimicrobial agent or an antibiotic.

Claim 214. (new) The method of Claim 1, wherein the medicant is an immunotoxin or immunosuppressant

Claim 215. (new) The method of Claim 1, wherein the medicant is a boron compound.

Claim 216. (new) The method of Claim 1, wherein the medicant is an ischemia-protective agent.

Claim 217. (new) The method of Claim X, wherein the ischemia-protective agent is N-methyl-D-aspartate (NMDA) receptor antagonist.

Claim 218. (new) The method of Claim 1, wherein the medicant is an adrenergic agent.

Claim 219. (new) The method of Claim 1, wherein the medicant is an anticonvulsant.

Claim 220. (new) The method of Claim 1, wherein the medicant is an anti-trauma agent.

Claim 221. (new) The method of Claim 1, wherein the medicant is cisplatin or carboplatin.

Claim 222. (new) The method of Claim 1, wherein the medicant is methotrexate.

Claim 224. (new) The method of Claim 1, wherein the medicant is 5-flourouracil.

Claim 224. (new) The method of Claim 1, where the medicant is amphotericin.

Claim 225. (new) The method of Claim 1, wherein the medicant is daunorubicin.

Claim 226. (new) The method of Claim 1, wherein the medicant is doxorubicin.

Claim 227. (new) The method of Claim 1, wherein the medicant is vincristine.

Claim 228. (new) The method of Claim 1, wherein the medicant is vinblastine.

Claim 229. (new) The method of Claim 1, wherein the medicant is busulfan.

Claim 230. (new) The method of Claim 1, wherein the medicant is chlorambucil.

Claim 231. (new) The method of Claim 1, wherein the medicant is cyclophosphamide.

Claim 232. (new) The method of Claim 1, wherein the medicant is melphalan.

Claim 233. (new) The method of Claim 1, wherein the medicant is ethyl ethanesulfonic acid.

Claim 234. (new) The method of Claim 1, wherein the medicant is a diagnostic agent

Claim 235. (new) The method of Claim 48, wherein the direct agonist of an ATP-sensitive potassium channel is minoxidil or minoxidil sulfate.

Claim 236. (new) The method of Claim 48, wherein the direct agonist is cromakalim.

Claim 237. (new) The method of Claim 48, wherein the direct agonist is levcromakalim.

Claim 238. (new) The method of Claim 48, wherein the direct agonist is pinacidil.

Claim 239. (new) The method of Claim 48, wherein the direct agonist is diazoxide.

Claim 240. (new) The method of Claim 48, wherein the medicant is administered via intravenous, intramuscular, intra-arterial, or intracarotid injection or infusion.

Claim 241. (new) The method of any Claim 48, wherein the agonist and the medicant are administered via intracarotid infusion or injection.

Claim 242. (new) The method of Claim 48, wherein the medicant is a protein.

Claim 243. (new) The method of Claim 48, wherein the medicant is a monoclonal antibody or antigen-binding antibody fragment.

Claim 244. (new) The method of Claim 48, wherein the medicant is a cytokine, cytokine antagonist, or cytokine agonist.

Claim 245. (new) The method of Claim 48, wherein the medicant is an interferon.

Claim 246. (new) The method of Claim 48, wherein the medicant is an interleukin.

Claim 247. (new) The method of Claim 247, wherein the interleukin is interleukin 2.

Claim 248. (new) The method of Claim 48, wherein the medicant is transforming growth factor.

Claim 249. (new) The method of Claim 248, wherein the transforming growth factor is transforming growth factor-β.

Claim 250. (new) The method of Claim 48, wherein the medicant is tumor necrosis factor-a.

Claim 251. (new) The method of Claim 48, wherein the medicant is an antimicrobial agent or an antibiotic.

Claim 252. (new) The method of Claim 48, wherein the medicant is an immunotoxin or immunosuppressant.

Claim 253. (new) The method of Claim 48, wherein the medicant is a boron compound.

Claim 254. (new) The method of Claim 48, wherein the medicant is an ischemia-protective agent.

Claim 255. (new) The method of Claim 255, wherein the ischemia-protective agent is N-methyl-D-aspartate (NMDA) receptor antagonist.

Claim 256. (new) The method of Claim 48, wherein the medicant is an adrenergic agent.

Claim 257. (new) The method of Claim 48, wherein the medicant is an anticonvulsant.

Claim 258. (new) The method of Claim 48, wherein the medicant is an anti-trauma agent.

Claim 259. (new) The method of Claim 48, wherein the medicant is cisplatin or carboplatin.

Claim 260. (new) The method of Claim 48, wherein the medicant is methotrexate.

Claim 261. (new) The method of Claim 48, wherein the medicant is 5-flouroouracil.

Claim 262. (new) The method of Claim 48, where the medicant is amphotericin.

Claim 263. (new) The method of Claim 48, wherein the medicant is daunorubicin.

Claim 264. (new) The method of Claim 48, wherein the medicant is doxorubicin.

Claim 265. (new) The method of Claim 48, wherein the medicant is vincristine.

Claim 266. (new) The method of Claim 48, wherein the medicant is vinblastine.

Claim 267. (new) The method of Claim 48, wherein the medicant is busulfan.

Claim 268. (new) The method of Claim 48, wherein the medicant is chlorambucil.

Claim 269. (new) The method of Claim 48, wherein the medicant is cyclophosphamide.

Claim 270. (new) The method of Claim 48, wherein the medicant is melphalan.

Claim 271. (new) The method of Claim 48, wherein the medicant is ethyl ethanesulfonic acid.

Claim 272. (new) The method of Claim 48, wherein the medicant is a diagnostic agent

Claim 273. (new) The pharmaceutical composition of Claim 135, wherein the direct agonist is minoxidil or minoxidil sulfate.

Claim 274. (new) The method of Claim 135, wherein the direct agonist is cromakalim.

Claim 275. (new) The method of Claim 135, wherein the direct agonist is levcromakalim.

Claim 276. (new) The method of Claim 135, wherein the direct agonist is pinacidil.

Claim 277. (new) The method of Claim 135, wherein the direct agonist is diazoxide.

Claim 278. (new) The pharmaceutical composition of Claim 135, wherein the therapeutic cytotoxic agent is cisplatin or carboplatin.

Claim 279. (new) The pharmaceutical composition of Claim 135, wherein the therapeutic cytotoxic agent is methotrexate.

Claim 280. (new) The pharmaceutical composition of Claim 135, wherein the therapeutic cytotoxic agent is 5-fluoroureacil.

Claim 281. (new) The pharmaceutical composition of Claim 135, wherein the therapeutic cytotoxic agent is amphotericin.

Claim 282. (new) The pharmaceutical composition of Claim 135, wherein the anticancer chemotherapeutic agent is daunorubicin, doxorubicin, vincristine, vinblastine, busulfan, chlorambucil, cyclophosphamide, melphalan, or ethyl ethanesulfonic acid.

Claim 283. (new) A pharmaceutical composition comprising a combination of a direct agonist of an ATP- sensitive potassium channel formulated together in a pharmaceutically acceptable solution together with a drug for delivery by intravascular infusion or injection, wherein the drug is a antimicrobial agent, antibiotic, interferon, cytokine, cytokine agonist, cytokine antagonist, monoclonal antibody, antigen-binding antibody fragment, immunotoxin, immunosuppressant, ischemia-protective agent, adrenergic agent, boron compound, anti-convulsant, anti-trauma agent or diagnostic agent.

Claim 284. (new) A pharmaceutical composition comprising a combination of a direct agonist of an ATP- sensitive potassium channel formulated together in a pharmaceutically acceptable solution together with a drug for delivery by intravascular infusion or injection, wherein the drug is a naked DNA expression vector, protein, oligonucleotide or nucleotide analog.

Claim 285. (new) The kit of Claim 153, wherein the direct agonist is minoxidil or minoxidil sulfate.

Claim 286. (new) The kit of Claim 153, wherein the direct agonist is cromakalim, levcromakalim, pinacidil, or diazoxide.